WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



(51) International Application Published Under the Patent Cooperation Treaty			1)
(51) International Patent Classification 6: A61K 7/48 A1		(11) International Publication Number: WO 99/4	7117
	A1	(43) International Publication Date: 23 September 1999 (23.	.09.99
(21) International Application Number: PCT/US9 (22) International Filing Date: 12 March 1999 (1)		BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, C	(Utility
(30) Priority Data: 60/078,136 16 March 1998 (16.03.98)	τ	JS GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KC, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA	G, KP G, MK E, SG A. UG
(71) Applicant: THE PROCTER & GAMBLE CO. [US/US]; One Procter & Gamble Plaza, Cincing 45202 (US).	nati, O	KZ, MD, RU, TJ, TM), European patent (AT, BE, CF, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, N)	Y, KG H, CY L. PT
(72) Inventor: BISSETT, Donald, Lynn; 3925 Dust Cor Drive, Hamilton, OH 45011 (US).	mmand	er ML, MR, NE, SN, TD, TG).	i, Gw
(74) Agents: REED, T., David et al.; The Procter & Company, 5299 Spring Grove Avenue, Cincinn 45217-1087 (US).	Gamb ati, O	Published With international search report.	
		·	

(54) Title: SKIN MOISTURIZING COMPOSITIONS

(57) Abstract

The present invention relates to methods of improving skin moisturization or skin hydration, and more specifically, to methods improving the skin's absorptive and/or adsorptive capacity for water.

10

15

20

25

SKIN MOISTURIZING COMPOSITIONS

TECHNICAL FIELD OF THE INVENTION

The present invention relates to methods of improving skin moisturization or skin hydration, and more specifically, to methods improving the skin's absorptive and/or adsorptive capacity for water.

BACKGROUND OF THE INVENTION

Physiologically, the skin is composed of an external cellular layer called the stratum corneum, an underlying epidermal layer and the dermis. The stratum corneum, which varies in thickness from approximately 15 microns on the face and the backs of the hands to 500 microns on the soles of the feet and the palms of the hands, plays a significant role in controlling the level of moisture in the skin. It is composed of keratinized cells, a natural moisturizing factor and lipids. All of these function together as a protective coating, as well as a moisture barrier to retain moisture within the skin.

In the epidermal area, which lies below the stratum corneum, the cells of the skin undergo change from normal living cell structure to the keratinized layer of the corneum. During this change, some proteins, particularly involucrin, are crosslinked to become the envelop of the stratum corneum cell. These cells contain keratins, which are also produced in the epidermis, and when hydrated function to provide flexibility to the stratum corneum. Other proteins, particularly filaggrin, are broken down to products which are located in the stratum corneum cells and function as natural moisturizing compounds. Below the epidermal layer, lies the normal dermis of the skin, which holds and transports water to the epidermal area.

Water is extremely important to the proper physical condition and appearance of skin. Dry and chapped skin is largely the result of an insufficient level of moisture in the stratum corneum. Soft, pliable, flexible, healthy skin cannot be maintained in the absence of a proper level of moisture in the stratum corneum.

10

15

20

25

30

The level of moisture in the skin is dependent upon a number of factors. Among these are the water binding potential of the stratum corneum, the rate at which water is supplied to the internal layers of the stratum corneum, and the rate at which water is lost from the external surface of the skin. With these factors in mind, investigators have, for a number of years, been actively searching for ways to maintain such proper levels of moisture in the skin.

Traditional methods of maintaining moisture in skin have involved the use of occlusive agents. Occlusives are hydrophobic substances that promote water retention by forming a barrier on the skin that will prevent moisture loss. The most commonly used occlusive agents include petrolatum, lanolin, cocoa butter, mineral oil and silicones.

Despite existence of such traditional methods of moisturizing skin, there remains a need for skin moisturization products which hydrate the skin by mechanisms other than occlusion. The present inventors have discovered that Vitamin B₃ compounds are effective in providing moisture or hydration to the skin by improving the adsorption of water onto stratum corneum or the absorption of water into stratum corneum. Specifically, it has been found that Vitamin B₃ compounds improve the production of the stratum corneum cell envelop, stratum corneum keratins, natural moisturizing factor precursor (filaggrin), and natural moisturizing factors which promote the skin's ability to take up and bind water.

It is, therefore, an object of the present invention to provide methods of moisturizing the skin.

Another object of the present invention is to provide methods of improving the skin's adsorptive and/or absorptive capacity for water by applying a safe and effective amount of a composition containing a vitamin B₃ compound.

These and other objects will become readily apparent from the detailed description which follows.

SUMMARY OF THE INVENTION

The present invention relates to methods of moisturizing or hydrating the skin by improving the adsorption of water to, and/or improving the absorptive capacity for water of mammalian skin, especially the epidermis and more especially the

10

15

20

stratum corneum of mammalian skin, by applying topically a safe and effective amount of a skin care composition comprising:

- A. a water adsorption or water absorption enhancing agent selected from the group consisting of vitamin B₃ compounds and mixtures thereof, and
- B. a dermatologically acceptable carrier for said vitamin B₃ compound.

The present invention further relates to articles of manufacture comprising a skin care composition comprising from about 0.1% to about 40% of a vitamin B₃ compound in a package for said skin care composition in association with the information about and/or instructions on the use of vitamin B₃ compounds to improve skin moisturization or hydration

Unless otherwise indicated, all percentages and ratios used herein are by weight of the total composition. All weight percentages, unless otherwise indicated, are on an actives weight basis. All measurements made are at approximately 25°C, unless otherwise designated. As used herein the terms "moisturization", "moisturized", "hydration" or "hydrated" broadly mean treatment or prevention of dry, flaky, scaly, tight, itchy skin to yield a smoother, softer skin as perceived by visual and/or tactile and/or sensorial assessments. As used herein the terms "absorb" or "absorption" broadly mean absorption of water into the skin, in particular into the epidermis and more particularly into the stratum corneum. As used herein the terms "adsorb" or "adsorption" broadly mean adsorption of water onto the skin, particularly onto the proteins of the epidermis and more particularly of the stratum corneum. The term "safe and effective amount" as used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive skin appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to provide a reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan.

30

25

DETAILED DESCRIPTION OF THE INVENTION

The skin moisturizing compositions of the present invention can comprise, consist of, or consist essentially of the essential elements and limitations of the

10

15

20

25

invention described herein, as well any of the additional or optional ingredients, components, or limitations described herein. <u>ESSENTIAL COMPONENTS</u>

<u>Vitamin B₃ component</u>

The compositions of the present invention comprise a safe and effective amount of a natural or synthetic vitamin B_3 compound. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably greater than 1% to about 50%, even more preferably greater than 2% to about 40%, and still more preferably greater than 5% to about 30%, most preferably greater than 10% to about 20%, of the vitamin B_3 compound.

As used herein, "vitamin B₃ compound" means a compound having the formula:

$$\bigcap_{N}$$

wherein R is - CONH₂ (i.e., niacinamide), - COOH (i.e., nicotinic acid) or - CH₂OH (i.e., nicotinyl alcohol); derivatives thereof; and salts of any of the foregoing.

Exemplary derivatives of the foregoing vitamin B₃ compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids, nicotinic acid N-oxide and niacinamide N-oxide.

Suitable esters of nicotinic acid include nicotinic acid esters of C₁-C₂₂, preferably C₁-C₁₆, more preferably C₁-C₆ alcohols. The alcohols are suitably straight-chain or branched chain, cyclic or acyclic, saturated or unsaturated (including aromatic), and substituted or unsubstituted. The esters are preferably non-rubifacient. As used herein, "non-rubifacient" means that the ester does not commonly yield a visible flushing response after application to the skin in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds may cause vasodilation not visible to the naked eye). Alternatively, a nicotinic acid material which is rubifacient at higher doses could be used at a lower dose at which a rubifacient response does not occur.

10

Non-rubifacient esters of nicotinic acid include, but are not limited to, tocopherol nicotinate and inositol hexanicotinate; tocopherol nicotinate is preferred.

Other derivatives of the vitamin B₃ compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of derivatives of niacinamide useful herein include nicotinyl amino acids, derived, for example, from the reaction of an activated nicotinic acid compound (e.g., nicotinic acid azide or nicotinyl chloride) with an amino acid, and nicotinyl alcohol esters of organic carboxylic acids (e.g., C1 - C18). Specific examples of such derivatives include nicotinuric acid and nicotinyl hydroxamic acid, which have the following chemical structures:

nicotinyl hydroxamic acid:

15

20

Exemplary nicotinyl alcohol esters include nicotinyl alcohol esters of the carboxylic acids salicylic acid, acetic acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of vitamin B₃ compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methylnicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzylnicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptonicotinic acid, nicomol, and niaprazine.

25

Examples of the above vitamin B₃ compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical

10

15

20

25

Company (St. Louis, MO); ICN Biomedicals, Inc. (Irvin, CA) and Aldrich Chemical Company (Milwaukee, WI).

One or more vitamin B_3 compounds may be used herein. Preferred vitamin B_3 compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

When used, salts, derivatives, and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating skin condition described herein.

Salts of the vitamin B₃ compound are also useful herein. Nonlimiting examples of salts of the vitamin B₃ compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide, carbonate, preferably chloride), and organic carboxylic acid salts (including mono-, di- and tri- C1 - C18 carboxylic acid salts, e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the vitamin B₃ compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic and D-Isoascorbic Acid with Nicotinic Acid and Its Amide", J. Organic Chemistry, VOL. 14, 22-26 (1949), which is incorporated herein by reference. Wenner describes the synthesis of the ascorbic acid salt of niacinamide.

In a preferred embodiment, the ring nitrogen of the vitamin B₃ compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the skin becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the vitamin B₃ compound is essentially uncomplexed. Therefore, if the composition contains the vitamin B₃ compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the skin. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility can be readily determined by one having ordinary skill in the art.

10

15

20

25

30

More preferably the vitamin B₃ compound is substantially uncomplexed in the composition prior to delivery to the skin. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the vitamin B₃ compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the vitamin B₃ compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill in the art.

Thus, in a preferred embodiment, the vitamin B₃ compound contains a limited amount of the salt form and is more preferably substantially free of salts of a vitamin B₃ compound. Preferably the vitamin B₃ compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The vitamin B₃ compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about 50% of the salt form.

The vitamin B₃ compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The vitamin B₃ compound is preferably substantially pure, more preferably essentially pure.

Without being limited by theory, it is believed that vitamin B₃ compounds increase skin moisturization or hydration by several different mechanisms. One mechanism involves the affect of vitamin B₃ compounds on natural moisturizing factors. Natural moisturizing factors include the water-binding, metabolic byproducts of skin proteins, especially filaggrin. It is believed that vitamin B₃ compounds increase the level of the above mentioned skin proteins, thereby increasing the level of natural moisturizing factors and, thus, moisturization. Another mechanism involves the effect of vitamin B₃ compounds on the level and/or molecular weight of keratin proteins in the stratum corneum. These proteins bind water and aid in providing flexibility to the corneum cell layer. Increased keratin level, thus, increases the concentration of moisture-binding proteins, resulting in improved skin moisturization. The degree of skin moisturization attained is also related to the type

10

15

20

25

30

of keratin present. Keratin proteins of higher molecular weights (i.e., molecular weights above _____) tend to bind more water. A third mechanism involves the effect of Vitamin B₃ compounds on the level of involucrin and desmosomal proteins. Involucrin is a protein precursor to the stratum corneum cell envelop which encases the keratin proteins and natural moisturizing factors. Desmosomal proteins are in close association with the stratum corneum cell envelop and aid in connecting the stratum corneum cells. Increased involucrin and the desmosomal protein levels augment and strengthen the corneum cell envelope, helping to retard the dehydration of the encased keratins and natural moisturizing factors and, thereby, improving skin moisturization.

Carrier

Another essential ingredient of the present invention is a dermatologically acceptable carrier. The phrase "dermatologically -acceptable carrier", as used herein, means that the carrier is suitable for topical application to the skin, has good aesthetic properties, is compatible with the actives of the present invention and any other components, and will not cause any untoward safety or toxicity concerns A safe and effective amount of carrier is from about 50% to about 99.99%, preferably from about 99.9% to about 80%, more preferably from about 98% to about 90%, most preferably from about 95% to about 90% of the composition.

The carrier can be in a wide variety of forms. For example, emulsion carriers, including, but not limited to, oil-in-water, water-in-oil, water-in-oil-in-water, and oil-in-water-in-silicone emulsions, are useful herein. These emulsions can cover a broad range of viscosities, e.g., from about 100 cps to about 200,000 cps. These emulsions can also be delivered in the form of sprays using either mechanical pump containers or pressurized aerosol containers using conventional propellants. These carriers can also be delivered in the form of a mousse. Other suitable topical carriers include anhydrous liquid solvents such as oils, alcohols, and silicones (e.g., mineral oil, ethanol, isopropanol, dimethicone, cyclomethicone, and the like); aqueous-based single phase liquid solvents (e.g., hydro-alcoholic solvent systems); and thickened versions of these anhydrous and aqueous-based single phase solvents (e.g., where the viscosity of the solvent has been increased to form a solid or semi-solid by the addition of

10

15

20

25

30

appropriate gums, resins, waxes, polymers, salts, and the like). Examples of topical carrier systems useful in the present invention are described in the following four references all of which are incorporated herein by reference in their entirety: "Sun Products Formulary" Cosmetics & Toiletries, vol. 105, pp. 122-139 (December 1990); "Sun Products Formulary", Cosmetics & Toiletries, vol. 102, pp. 117-136 (March 1987); U.S. Patent No. 4,960,764 to Figueroa et al., issued October 2, 1990; and U.S. Patent No. 4,254,105 to Fukuda et al., issued March 3, 1981.

The carriers of the skin care compositions can comprise from about 50% to about 99% by weight of the compositions of the present invention, preferably from about 75% to about 99%, and most preferably from about 85% to about 95%.

Preferred cosmetically and/or pharmaceutically acceptable topical carriers include hydro-alcoholic systems and oil-in-water emulsions. When the carrier is a hydro-alcoholic system, the carrier can comprise from about 0% to about 99% of ethanol, isopropanol, or mixtures thereof, and from about 1% to about 99% of water. More preferred is a carrier comprising from about 5% to about 60% of ethanol, isopropanol, or mixtures thereof, and from about 40% to about 95% of water. Especially preferred is a carrier comprising from about 20% to about 50% of ethanol, isopropanol, or mixtures thereof, and from about 50% to about 80% of water. When the carrier is an oil-in-water emulsion, the carrier can include any of the common excipient ingredients for preparing these emulsions. A more detailed discussion of suitable carriers is found in U.S. Patent 5,605,894 to Blank et al., and, U.S. Patent 5,681,852 to Bissett, both of which are herein incorporated by reference in their entirety.

OPTIONAL COMPONENTS

The moisturizing compositions of the present invention may optionally include a film-forming agent or substantivity enhancer. The film-forming agent or substantivity enhancer of the present invention is, generally, an organic polymer or resin which is soluble in the carrier and which during carrier evaporation will form a relatively thin film on the skin, thereby enhancing the substantivity of the vitamin B₃ compound. The film-forming agent or substantivity enhancer can be natural or synthetic. Suitable film-forming agents or substantivity enhancers include, but are not

10

15

20

25

30

limited to, polyvinyl alcohol, ethyl cellulose, methoxy cellulose, hydroxyethyl cellulose, nitrocellulose, beegum, polyvinylpyrrolidone, vinylpyrrolidone/vinyl acetate copolymers, copolymers of eicosene and vinyl pyrrolidone (an example of which is available from GAF Chemical Corporation as Ganex.RTM. V-220), vinyl acetate/unsaturated carboxylic acid copolymers, terpolymers of methyl methacrylate/stearyl methacrylate/dimethylaminoethyl methacrylate, terpolymers of vinyl acetate/allyl stearate/allyloxyacetic acid, and maleic anhydride/methyl vinyl ether copolymers such as those commercially referred to as "Gantrez AN" as well as the ethyl, isopropyl and butyl esters of these copolymers, and maleic anhydride/butyl vinyl ether copolymers.

Plasticizing agents desirably are added to the composition to impart flexibility to the polymer film. Suitable plasticizing agents include, but are not limited to, polyethylene glycol, polyoxyethylene propylene glycol, polyoxypropylene glycol, polyoxyethylene polyoxypropylene block copolymers, glycerin and various vegetable oils such as cottonseed oil, palm oil, rapeseed oil, sunflower oil, castor oil, and the like. In the preparation and examination of film forming polymers, it known that the rate of release of the active from the polymer film depends upon the nature of the plasticizing agent used. Hydrophobic plasticizing agents, such as the vegetable oils, tended to impede the rate of release of the active substance while the hydrophilic materials such as polyoxypropylene glycol, polyethylene glycols and polyoxyethylene tended to enhance the rate of release of the active substance from the film.

The moisturizing compositions of the present invention may optionally comprise additional skin actives. Non-limiting examples of such skin actives include hydroxy acids such as salicylic acid; desquamatory agents such as zwitterionic surfactants; sunscreens such as 2-ethylhexyl-p-methoxycinnamate, 4,4'-t-butyl methoxydibenzoyl-methane, octocrylene, phenyl benzimidazole sulfonic acid; sunblocks such as zinc oxide and titanium dioxide; anti-inflammatory agents; anti-oxidants/radical scavengers such as tocopherol and esters thereof; metal chelators, especially iron chelators; retinoids such as retinol, retinyl palmitate, retinyl acetate, retinyl propionate, and retinal; N-acetyl-L-cysteine and derivatives thereof; hydroxy acids such as glycolic acid; keto acids such as pyruvic acid; benzofuran derivatives;

10

15

20

25

30

and skin protectants. Mixtures of any of the above mentioned skin actives may also be used. A more detailed description of these actives is found in U.S. Patent 5,605,894 to Blank et al. (previously incorporated by reference). Preferred skin actives include hydroxy acids such as salicylic acid, sunscreen, antioxidants and mixtures thereof.

Other conventional skin care product additives may also be included in the compositions of the present invention. For example, urea, guanidine, glycerol, petrolatum, mineral oil, sugar esters and polyesters, polyolefins, methyl isostearate, ethyl isostearate, cetyl ricinoleate, isononyl isononanoate, isohexadecane, lanolin, lanolin esters, cholesterol, pyrrolidone carboxylic acid/salt (PCA), trimethyl glycine (betaine), transexamic acid, amino acids (e.g., serine, alanine) and/or their salts, panthenol and its derivatives, collagen, hyaluronic acid, elastin, hydrolysates, primrose oil, jojoba oil, epidermal growth factor, soybean mucopolysaccharides, and mixtures thereof may be used. Other suitable additives or skin actives are discussed in further detail in PCT application WO 97/39733, published October 30, 1997, to Oblong et al., herein incorporated by reference in its entirety.

Preparation of Skin Moisturizing Compositions

The compositions of the present invention are generally prepared by conventional methods such as are known in the art of making topical compositions. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, application of vacuum, and the like. Non-limiting examples of the product form can be a gel, emulsion, lotion, cream, liquid, solution, ointment, etc.

Methods of Moisturizing Skin

The methods of the present invention are useful for moisturizing or hydrating mammalian skin (especially human skin, especially human facial and body skin, more especially human hand, leg, and facial skin), especially the epidermis and more especially the stratum conreum of mammalian skin. The skin moisturization or hydration methods of the present invention involve topically applying to the skin a safe and effective amount of the skin moisturizing or hydrating composition of the

10

15

20

25

30

present invention. The amount of the composition which is applied, the frequency of application and the period of use will vary widely depending upon the level of vitamin B₃ compound and/or other components of a given composition and the level of moisturization or hydration desired. However, to achieve the moisturization or hydration benefits of the present invention, the skin moisturizing or hydrating composition must be applied so as to provide a constant minimum vitamin B₃ concentration on the skin of from about 0.001 mg/cm2 to about 1 mg/cm2. The term "constant", as used herein, means the level of the vitamin B₃ compound on the skin does not vary below the minimum concentration by more than about 20%, preferably by more than about 10% over about a 1-12 hour time period. The constant level can be achieved by reapplication of product to skin, especially to areas of the body which are often washed during the day, such as face and hands.

In a preferred embodiment, the composition is chronically applied (or reapplied such as after washing) to the skin. By "chronic topical application" is meant continued topical application of the composition over an extended period during the subject's lifetime, preferably for a period of at least about one week, more preferably for a period of at least about two weeks, even more preferably for a period of at least about three months, even more preferably for at least about three months, even more preferably for at least about one year. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that chronic application continue throughout the subject's lifetime to maintain and/or increase the benefits achieved. Typically applications would be on the order of one to about four times per day over such extended periods, however application rates can be more than four times per day, especially for use on areas of the body which are often washed during the day, such as face and hands.

A wide range of quantities of the compositions of the present invention can be employed to provide a skin appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm² skin, from about 0.1 mg/cm² to about 10 mg/cm². A particularly useful application

10

15

20

25

amount is about 1 mg/cm² to about 4 mg/cm², a more particularly useful application amount being about 2 mg/cm².

Regulating skin condition is preferably practiced by applying a composition in the form of a skin lotion, cream, cosmetic, or the like which is intended to be left on the skin for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). After applying the composition to the skin, it is preferably left on the skin for a period of at least about 5 minutes, more preferably at least about 20 minutes, even more preferably at least about 1 hour, most preferably for at least several hours, e.g., up to about 12 hours, before removal, e.g., by washing.

Another approach to ensure a continuous exposure of the skin to at least a minimum level of vitamin B3 compound is to apply the compound by use of a patch. Such an approach is particularly useful for problem skin areas needing more intensive treatment. The patch can be occlusive, semi-occlusive or non-occlusive. The vitamin B3 compound composition can be contained within the patch or be applied to the skin prior to application of the patch. The patch can also include additional actives such as chemical initiators for exothermic reactions such as those described in PCT application WO 9701313 to Burkett et al. Preferably the patch is applied (e.g., to the face) at night as a form of night therapy.

EXAMPLES

The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention.

Example 1

The following is an example of a skin cream incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to to the skin from about from about 0.5 g to about 50g.

30

Ingredient

% Weight

Glycerine	6.933
Niacinamide	5.000
Permethyl 101A 1	3.000
Sepigel ²	2.500
Q2-1403 ³	2.000
Isopropyl Isostearate	1.330
Arlatone 2121 ⁴	1.000
Cetyl Alcohol CO-1695	0.720
SEFA Cottonate 5	0.670
Tocopherol Acetate	0.500
Panthenol	0.500
Adol 62 6	0.480
Kobo Titanium Dioxide	0.400
Sodium Hydroxide 50%	0.0125
Aqueous	
Fiery 5 ⁷	0.150
Disodium EDTA	0.100
Glydant Plus 8	0.100
Myrj 59 9	0.100
Emersol 132 ¹⁰	0.100
Color	0.00165
Purified Water	q.s. to 100

Example 2

The following is an example of a skin cream incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to to the skin from about from about 0.5 g to about 50g.

<u>Ingredient</u>	% Weight
Glycerine	6.933

Tocopherol nicotinate	2.000
Permethyl 101A 1	3.000
Sepigel ²	2.500
Q2-1403 ³	2.000
Isopropyl Isostearate	1.330
Arlatone 2121 ⁴	1.000
Cetyl Alcohol CO-1695	0.720
SEFA Cottonate 5	0.670
Tocopherol Acetate	0.500
Panthenol	0.500
Adol 62 ⁶	0.480
Kobo Titanium Dioxide	0.400
Sodium Hydroxide 50%	0.0125
Aqueous	
Fiery 5 ⁷	0.150
Disodium EDTA	0.100
Glydant Plus 8	0.100
Myrj 59 9	0.100
Emersol 132 10	0.100
Color	0.00165
Purified Water	q.s. to 100

Example 3

The following is an example of a skin cream incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to to the skin from about from about 0.5 g to about 50g.

Ingredient	% Weight
Glycerine	6.933
Niacinamide	2.000
Permethyl 101A 1	4.000
Q2-1403 ³	2.000
Isopropyl Isostearate	1.330
Arlatone 2121 ⁴	1.000
Cetyl Alcohol CO-1695	0.720
SEFA Cottonate 5	0.670
Carbopol 954 ¹¹	0.500
Tocopherol Acetate	0.500
Panthenol	0.500
Adol 62 ⁶	0.480
Kobo Titanium Dioxide	0.400
Sodium Hydroxide 50%	0.250
Aqueous	
Fiery 5 ⁷	0.150
Disodium EDTA	0.100
Glydant Plus 8	0.100
Myrj 59 ⁹	0.100
Emersol 132 10	0.100
Carbopol 1382 ¹²	0.100
Color	0.00165
Purified Water	q.s. to 100

- 1. Isohexadecane, Presperse Inc., South Plainfield, NJ
- 2. Polyacrylamide(and)C13-14 Isoparaffin(and)Laureth-7, Seppic Corporation, Fairfield, NJ
- 3. dimethicone(and)dimethiconol, Dow Corning Corp., Midland,

МІ

- 4. Sorbitan Monostearate and Sucrococoate, ICI Americas Inc., Wilmington, DE
- 5. Sucrose ester of fatty acid, Procter and Gamble, Cincinnati, OH
- 6. Stearyl Alcohol, Procter and Gamble, Cincinnati, OH
- 7. Fiery 5 n/a, Procter and Gamble, Cincinnati, OH
- 8. DMDM Hydantoin (and) Iodopropynyl Butylcarbamate, Lonza Inc., Fairlawn, NJ
- 9. PEG-100 Stearate, ICI Americas Inc., Wilmington, DE
- 10. Stearic acid, Henkel Corp., Kankakee, IL
- 11. Carbomer, BF Goodrich, Cleveland OH
- 12. Carbomer, BF Goodrich, Cleveland OH

10

SDOCID: ~WO

00/711741 1 -

10

WHAT IS CLAIMED IS:

- 1. A method of adsorbing water to or absorbing water into mammalian skin by applying to the skin a safe and effective amount of a skin care composition comprising:
 - A. a water adsorption or water absorption enhancing agent selected from the group consisting of vitamin B₃ compounds and mixtures thereof; and
 - B. a dermatologically acceptable carrier for said vitamin B₃ compound.
- 2. A method according to Claim 1, wherein the water adsorption or absorption is produced by increasing the concentration level of skin proteins selected from the group consisting of filaggrin, keratin, involucrin, and mixtures thereof.
- 15 3. A method according to any one of the preceding Claims, wherein the concentration of the adsorption or absorption enhancing agent is greater than 5%.
- 4. A method according to any one of the preceding Claims, wherein said vitamin
 B₃ compound is selected from niacinamide, derivatives of niacinamide, non vasodilating esters of nicotinic acid, and mixtures thereof.
 - 5. A method according to any one of the preceding Claims, wherein the composition further comprises an additional skin active selected from the group consisting of hydroxy acids, desquamatory agents, sunscreens, anti-oxidants, retinoids and mixtures thereof.
- A method according to any one of the preceding Claims, wherein the hydroxy acid is salicylic acid; the desquamatory agent is selected from the group consisting of zwitterionic surfactants and mixtures thereof; the sun-block is selected from the group consisting of zinc oxide, titanium dioxide and mixtures thereof; the sunscreen is selected from the group consisting of 2-ethylhexyl-p-methoxycinnamate, 4,4'-t-butyl methoxydibenzoyl-methane, phenyl benzimidazole sulfonic acid, octocrylene and mixtures thereof; the anti-oxidant is selected from the group consisting of tocopherol, esters

thereof and mixtures thereof; and the retinoid is selected from the group consisting of retinol, retinyl acetate, retinyl propionate, and mixtures thereof.

- A method of moisturizing or hydrating mammalian skin, comprising applying a safe and effective amount of a skin care composition comprising:
 - a. a safe and effective amount of at least one vitamin B₃ compound;
 - b. a cosmetically acceptable carrier;
- such that a minimum concentration of from 0.001 mg/cm2 to 1 mg/cm2 of the Vitamin B₃ compound is maintained on the skin.
 - 8. A method according to any one of the preceding Claims, wherein the minimal skin concentration of the vitamin B₃ compound is achieved by repeated application of the skin composition.
- 45 9. A method according to any one of the preceding Claims, wherein the skin care composition further comprises a film-forming agent or substantivity enhancer.
- 10. An article of manufacture comprising a skin care composition comprising from 0.1% to 40% of a vitamin B₃ compound in a package for said skin care composition in association with the information about and/or instructions on

INTERNATIONAL SEARCH REPORT

Inter nal Application No

PCT/US 99/05413 . CLASSIFICATION OF SUBJECT MATTER PC 6 A61K7/48 IPC 6 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X PATENT ABSTRACTS OF JAPAN 1,2,5,10 vol. 11, no. 353 (C-457), 18 November 1987 & JP 62 126106 A (KANEBO LTD.). 8 June 1987 see abstract Υ 5,6 Y WO 97 39733 A (THE PROCTER & GAMBLE 5,6 COMPANY) 30 October 1997 cited in the application see the whole document X 10 PATENT ABSTRACTS OF JAPAN Х 1,2,10 vol. 11, no. 365 (C-460), 27 November 1987 & JP 62 138410 A (KANEBO LTD.), 22 June 1987 see abstract X Further documents are listed in the continuation of box C. χ Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 19 May 1999 02/06/1999 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

1

Alvarez Alvarez, C

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/US 99/05413

C /Continu	PCT/US 99/05413			
Category °	(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT ategory Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No			
	oration of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	Relevant to claim No.	
X	PATENT ABSTRACTS OF JAPAN vol. 11, no. 349 (C-456), 14 November 1987 & JP 62 123106 A (KANEBO LTD.), 4 June 1987 see abstract	1,2,10		
А	WENNINGER AND MCEVEN: "International Cosmetic Ingredient Dictionary and Handbook. Volume 1" 1997, THE COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION, WASHINGTON, DC USA XP002103086 see page 848 "Niacinamide"	4		
		·		
-				

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern .al Application No PCT/US 99/05413

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9739733 A	30-10-1997	AU 3114697 A AU 3115097 A CZ 9803422 A EP 0896522 A WO 9739734 A	12-11-1997 12-11-1997 17-02-1999 17-02-1999 30-10-1997